

**CASE REPORT**

Food/farmed animals

# Use of antimicrobial impregnated calcium sulphate beads in the surgical management of mandibular osteomyelitis in an 8-year-old huacaya alpaca

Eleonora Po<sup>1</sup>  | Matthew James Allen<sup>1</sup> | Richard G. Whitlock<sup>2</sup> | Sara Hassouna Elsayed<sup>1</sup><sup>1</sup> Department of Veterinary Medicine, University of Cambridge, Cambridge, UK<sup>2</sup> Grove Referrals, Grove House, Fakenham, Norfolk, UK**Correspondence**Eleonora Po, University of Cambridge, Department of Veterinary Medicine, Madingley Rd, Cambridge, CB3 0ES, UK.  
Email: ep528@cam.ac.uk**Abstract**

An 8-year-old, male huacaya alpaca presented for a left mandibular swelling that was not responsive to antimicrobial treatment. A computed tomography scan was obtained, confirming the presence of a lytic bone destruction and primary mandibular osteomyelitis. Surgical debridement of the area was performed and the surgical site was packed with antibiotic-loaded calcium sulphate beads to provide local antibiotic delivery and support new bone formation. The surgical intervention and implantation of the beads were well tolerated, and no postsurgical issues were reported over the following 12 months. A follow-up computed tomography scan was performed 14 months after surgery and this revealed near-complete restoration of bone architecture and no evidence of active bone destruction. A combination of surgical debridement and antibiotic-loaded calcium sulphate beads is a viable and cost-reasonable option for the treatment of osteomyelitis in camelids.

**BACKGROUND**

Osteomyelitis is a debilitating disease that is commonly seen in veterinary practice. In camelids, osteomyelitis has been reported secondary to trauma,<sup>1</sup> after orthopaedic surgery<sup>2</sup> or as a consequence of haematogenous spread of infection,<sup>3</sup> and is a common finding in the appendicular and axial skeleton of camelids.<sup>4,5</sup> Osteomyelitis of the maxillofacial area has been reported in camelids and can occur as primary event or secondary to dental disease, particularly tooth root abscesses.<sup>6,7</sup> In camelids, irrespective of the underlying aetiology, osteomyelitis of the maxillofacial area occurs most commonly in the mandible. Clinical signs of facial swelling, pain on palpation of the affected area and an externally visible draining tract (cloaca) characterise these cases.

Osteomyelitis is usually accompanied by bone sclerosis, new alveolar bone formation, and osseous sequestration can be a common sequela.<sup>8</sup> For the correct identification of these changes, radiography and computed tomography (CT) are auxiliary imaging modalities, which can provide useful additional clinical information. Although primary and secondary osteomyelitis have a similar radiographic appearance, with bone sclerosis and new alveolar bone formation, the changes affect different structures, with more localised changes over the affected tooth in the case of a tooth abscess versus more generalised changes in the case of primary osteomyelitis.

Treatment of primary or secondary osteomyelitis (and periapical infections) is either medical, surgical or a combination

of both. Medical treatment of osteomyelitis usually includes the use of antimicrobials and nonsteroidal anti-inflammatory drugs. When selecting the most appropriate antimicrobial for treating these cases, a number of factors must be considered. In addition to antimicrobial sensitivity and target, the ability of the antibiotic to penetrate into the infected bone and the propensity of the microorganism to form a biofilm and resist the effect of the antibiotic are fundamental considerations.<sup>8</sup> Antibiotics are typically administered for extended periods of time, often between 2 and 6 weeks,<sup>6</sup> to ensure complete elimination of the infection. These extended courses of treatment can be challenging for both practical and economic reasons, as well as from the perspective of increasing the risk of adverse effects and the development of antimicrobial resistance.<sup>9</sup> The choice of antimicrobials can also vary depending on the availability of the drugs within a given country and the local regulations for prescribing. Ceftiofur sodium, procaine penicillin, florfenicol and isoniazid have been reported in the literature from North America.<sup>10</sup> In certain countries, such as the United Kingdom, alpacas are classified as farm animals and, as a consequence, it is more common to use first-line antimicrobials such as penicillins and florfenicols as the standard treatments, preserving critically important antimicrobials for cases that do not respond to the first-line drugs.

Surgical treatment may involve a combination of tooth surgery alone and/or bone curettage with removal of sequestra. Although the overall prognosis for survival after surgical management of sequestra is generally good,<sup>3</sup> it has been

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reported that around half of the cases that undergo surgery for tooth root abscesses go on to develop complications such as reinfection, presence of chronic draining tracts and chronic osteomyelitis.<sup>11</sup> It can be speculated that this could be due to incomplete elimination of infected bone, lack of antimicrobial penetration into the infected site, circulating septic emboli or excessive chronicity of the disease.

In the lead author's experience, working within a referral setting, camelids presenting with chronic extensive osteolytic facial lesions have a relatively poor prognosis due to increased fragility of the bone, leading to pathological fractures or recurrence of disease despite aggressive medical and surgical treatment.

Despite aggressive surgical debridement, the presence of residual infected and/or necrotic bone fragments constitute a risk for reinfection and may require repeated surgical interventions and prolonged antimicrobial therapy. Moreover, drastic removal of affected bone can create presence of 'dead space', which can fill in with blood and constitute a growth media for bacterial infection, hampering healing of bone.<sup>12</sup>

Several options may be available to limit reinfection. Careful surgical technique, especially as it relates to preserving blood supply and reduction of dead space, is mandatory. Intraoperative imaging (e.g., fluoroscopy) can be helpful in detecting residual bone fragments that need to be removed. Another approach is to provide a local source of antibiotics within and immediately adjacent to the infected site. Classically, this involves the use of antibiotic-loaded beads made by mixing powdered or liquid antibiotics with the acrylic polymer, polymethyl methacrylate (PMMA).<sup>13,14</sup> Although they can be effective, PMMA beads are nonresorbable and need to be removed at a second surgery. Additionally, the physical presence of PMMA within the wound site inhibits new bone formation. Most importantly, a number of studies have now shown that the elution of antibiotics from PMMA is a surface phenomenon, with early release followed by chronic low-level elution<sup>15,16</sup> leading to a risk of drug resistance.

Resorbable polymers, such as polylactic acid (PLA), polycaprolactone (PCL) and calcium-based bioceramics, such as calcium sulphate and calcium phosphate, represent a potentially attractive alternative to PMMA.<sup>15</sup> These materials can be mixed with antibiotics and then used either as an injectable paste or as solid beads or pellets that can be implanted in and around bone. The elution of antibiotics from these resorbable preparations is slower and more protracted, with local concentrations above the minimum inhibitory concentration for several weeks.<sup>17</sup> The material is typically resorbed by around 8 weeks post surgery,<sup>1,8</sup> removing the need for a secondary surgical intervention and providing a local source of calcium and phosphate ions for new bone formation while delivering the antibiotic of choice locally at the site of infection.

## CASE PRESENTATION

An 8-year-old, male, entire black huacaya alpaca was presented for investigation and management of severe swelling of the left mandibular region. The alpaca had an unremarkable prior health history, with routine vaccination targeting common environmental clostridial organisms, foot trimming, shearing and teeth care performed on farm.

## LEARNING POINTS/TAKE HOME MESSAGES

- Calcium sulphate beads were well tolerated within soft tissues and bone.
- Primary osteomyelitis had a good long-term outcome following surgical debridement with antibiotic-loaded calcium sulphate beads.
- This option can be considered in association with surgical dental extraction secondary to tooth root abscesses.
- Calcium sulphate, antibiotic-loaded beads are biocompatible, biodegradable and osteoinductive, allowing controlled local antibiotic release, which can be tailored to each patient's specific needs based on the results from antibiotic sensitivity testing. This makes it an ideal bone substitute material for implantation post osteomyelitis debridement surgery.

Two months before presentation at the clinic, a swelling was noticed on the mandible and was treated by the referring veterinarian with a combination of long-acting penicillin (20 mg/kg, SC, every 72 hours, 15-day course, Ultrapen LA, 30%, Norbrook, UK) and meloxicam (1 mg/kg, five consecutive doses, Loxicom 20 mg/ml, Norbrook, UK). Due to lack of response to therapy, the antibiotic was changed to florfenicol (20 mg/kg, SC, every 48 hours, Nuflor 300 mg/ml, MSD, UK) and the alpaca was referred for further investigation.

At the first examination in August 2018, the alpaca weighed 75.5 kg, its body condition score (BCS) was 4.5/10. Its vital parameters were within normal limits with a temperature of 37.1°C; pulse of 60 beats per minute and a respiratory rate of 28 breaths per minute. A 10 × 10 cm swelling was palpable at the left mandible with hard contours and a soft centre (Figure 1). The left mandibular lymph node was also enlarged and painful. No nasal discharge was noticed. The alpaca had maintained appetite despite the swelling; however, the owner reported longer than normal mastication (more time spent at the feed trough). No weight loss or increased competition with herd companions was reported.

## INVESTIGATIONS

A fine-needle aspirate confirmed the presence of a thick purulent exudate within the swelling. To diagnose the extent of mandibular disease, and any potential tooth involvement, a pre- and post-contrast (1 ml/kg, Ioxhol, Omnipaque, GE healthcare, UK) CT scan (16-slice scanner, Toshiba Aquilion 16) was performed under general anaesthesia. The CT scan revealed diffuse chronic osteomyelitis of the body and ramus of the left mandible, with several sequestra along the mandible (Figure 2; 3 left). No tooth lesion was noted, leading to a diagnosis of primary left mandibular osteomyelitis. In the post-contrast view, the left jugular vein appeared very distended and thick, likely indicative of phlebitis. There was marked soft tissue swelling of the area adjacent to the affected mandible, with many of these swellings containing focal mineralised material (Figure 2).



**FIGURE 1** The alpaca on admission after (presurgical) incision and drainage of the left mandibular mass



**FIGURE 2** Preoperative computed tomography (CT) scan section showing severe osteomyelitis of the left branch of the mandible and moth-eaten appearance of the surrounding bone. A chip can be seen (white arrow)

## TREATMENT

Due to the severity and the chronicity of the osteomyelitis, surgical debridement of the affected bone was considered the most appropriate treatment option. In view of the suspected phlebitis, the decision was made to delay surgery, pending

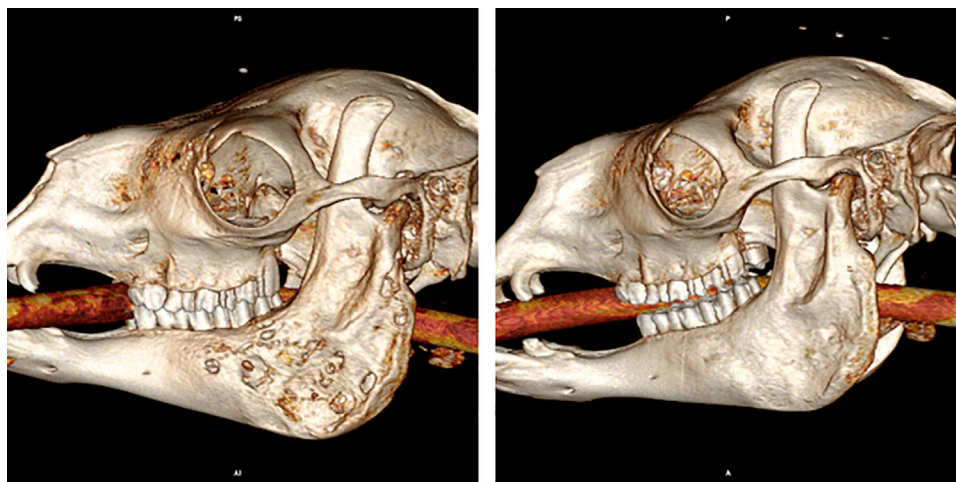
resolution of the phlebitis with florfenicol (20 mg/kg, subcutaneously (SC), q48 hours; Nuflor 200 mg/ml, MSD, UK) and meloxicam (1 mg/kg, IV, q48 hours; Metacam, Boehringer Ingelheim, UK). Omeprazole was also given for a total of 5 days (0.8 mg/kg, IV, TID; Starpharmacy Ltd, UK) for the prevention of gastric ulcers. Ahead of surgery, the mandibular swelling was incised to allow drainage of the purulent exudate, which was submitted for culture. The area was flushed topically with diluted povidone iodine (1%, Vetasept, Animal Care Group Ltd, York, UK) in preparation for surgical debridement, which was effective at partially reducing the local mandibular swelling.

This surgical procedure occurred 15 days after admission and with the informed consent of the owner. Under general anaesthesia as well as mandibular nerve block, the animal was positioned in lateral recumbency, the skin over the left mandible was clipped, cleaned with surgical antiseptic and draped for surgery. A vertical skin incision was performed over the ramus and the angle of the mandible, and subcutaneous (SC) tissues and muscle retracted to expose the mandible, taking care to avoid damage to the cranial nerves, parotid gland and main vessels. Although cultures from the wound exudate failed to grow any microorganisms, the site was considered to be infected and the affected bone was debrided using a high-speed burr until healthy bone was reached. A water-soluble antimicrobial, ceftiofur sodium (2.2 mg/kg, Excenel, Zoetis, UK) was mixed with a novel resorbable calcium sulphate matrix (Kerrier bead kits for veterinary orthopaedic infections, Kerrier, FL, USA) according to manufacturer's instructions to produce an antibiotic-loaded paste. The paste was moulded into beads that were packed into the defects in the bone. Additional beads were placed in adjacent soft tissues (Figure 4). The muscle layers were sutured in three layers using resorbable sutures of 2-0 polyglactin 910 (Vicryl; Johnson and Johnson) to close the dead space. A Penrose drain was placed to increase drainage of fluid during the days after surgery and skin was closed with nonresorbable polypropylene suture (Prolene; #1 Johnson and Johnson). Accurate positioning of the beads in and around the bone defects was confirmed with postoperative x-rays.

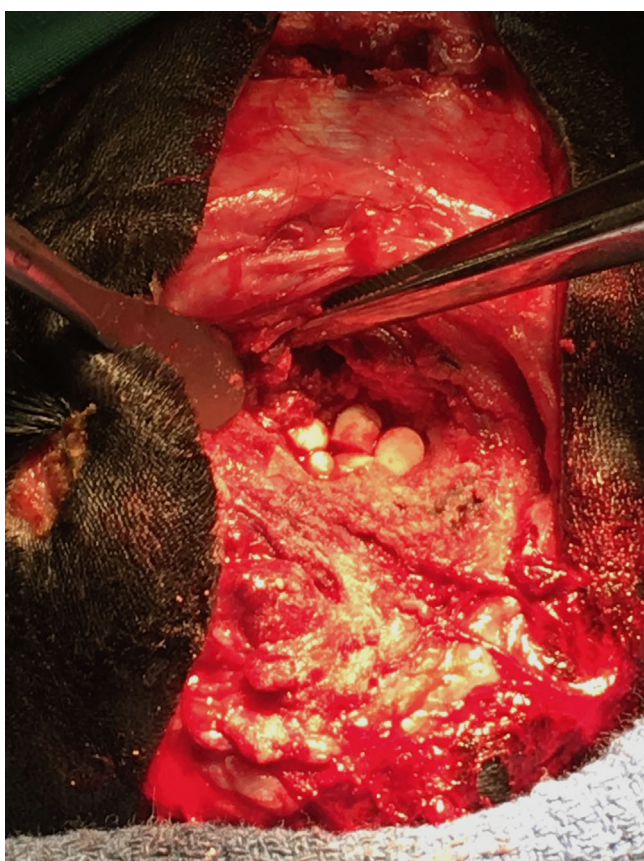
## OUTCOME AND FOLLOW-UP

Recovery from surgery and the early postoperative period were unremarkable, with the animal maintaining appetite, normal mentation and vital parameters. Medications administered until the day of discharge were (florfenicol: 20 mg/kg, SQ, q48 hours, 300 mg/ml, Nuflor, MSD, UK) and nonsteroidal anti-inflammatory drugs (meloxicam, IV, 1 mg/kg, q48 hours, Metacam, Boehringer Ingelheim, UK).

Swelling of the surgical site reduced progressively. The Penrose drain was removed on the third postoperative day. There was no discharge from the surgical incision, and although the incision and the local (left) mandibular lymph node were found to be sensitive to palpation on Day 7, this was transient and resolved by the postoperative Day 9, at which time the alpaca was discharged from the hospital with instructions for 2 more weeks of systemic antibiotics (florfenicol: 20 mg/kg, SQ, q48 hours, 300 mg/ml, Nuflor, MSD, UK). The owner was warned of the potential risk of long-term use of



**FIGURE 3** Left, preoperative lateral left-sided three-dimensional (3D) reconstruction of the jaw lesions before surgery. The moth-eaten appearance of the left mandible is noticeable and occupies the angle and the branch of the mandible. Right, lateral left-sided 3D reconstruction of the mandible at the recheck appointment, 14 months after surgery



**FIGURE 4** Intraoperative photograph illustrating the packing of the antibiotic-loaded calcium sulphate beads into the debrided regions of the mandible

florfenicol, related to the secondary effects reported by Holmes et al. (2012)<sup>9</sup> and was asked to monitor signs such as anorexia, depression and report any change in behaviour.

Telephone follow-up was conducted with the owner at 1 month post discharge, at which time the alpaca was reported to have normal appetite and behaviour. The surgical site was still slightly swollen, but no discharge or dehiscence were noticed. By 3 months, the owner reported that there was minimal residual visible swelling around the site.

The alpaca came back to the clinic at 14 months post surgery for clinical follow-up. The alpaca was 86 kg, with a

body condition score of 7/10. Vital parameters were within normal limits. Palpation of the left mandibular area revealed minimal callus, which was not sensitive to touch and lymph nodes were within normal limits. A repeat CT scan (including contrast) was obtained and this revealed a widening of the bone from the level of the left temporomandibular joint dorsally and extending to the ventral aspect of the mandible and slightly moth-eaten appearance of the trabecular bone of the left mandible with several small hyperattenuating specks within the soft tissues lateral to the flared aspect of the mandible, at the level where the antibiotic beads were previously introduced (Figure 3, right). The post-contrast CT revealed no contrast enhancement within the vessels of the head or the soft tissue structures of the head.

Telephone follow-up at 2 years post surgery confirmed that the alpaca had normal appetite and behaviour, with no visible recurrence of swelling or reinfection of the previously affected area.

## DISCUSSION

While acute osteomyelitis may go unnoticed, thorough examination of facial symmetry on routine assessment of the camelid may aid early diagnosis.<sup>7</sup> Medical treatment of early cases is usually successful, with antimicrobial therapy aimed at targeting good bone penetration and targeting causative bacteria, which are commonly anaerobes such as *Actinomyces* spp., *Actinobacillus* spp., *Escherichia coli*,<sup>11</sup> *Fusobacterium necrophorum*, *Staphylococcus aureus*, *Staphylococcus intermedius*, *Enterococcus* spp., *Pseudomonas* spp., *Bacillus* spp. and *Corynebacterium pseudotuberculosis*.<sup>3</sup>

Chronic cases like the one described in this case report have a worse prognosis and outcome and may be complicated by the extensive degree of bone damage, the presence of sequestra and by limited antimicrobial penetration into the affected area. While aggressive medical treatment is generally attempted in the field, frequently these cases are either referred for more investigation and surgical management, or euthanased due to lack of response to therapy or recurrence of disease.

Surgical management of chronic osteomyelitis cases secondary to periapical infections may be disappointingly unsuccessful. A retrospective case-based study involving 123 animals by Niehaus et al.<sup>11</sup> investigated perioperative complications of cases treated surgically for tooth root abscesses. Of this population, where follow-up was available (68 animals), 50% demonstrated complications, such as reinfection, presence of chronic draining tracts, osteomyelitis, sequestrums, sinusitis, cellulitis and mandibular fractures, leading in many cases to a second surgical intervention. In contrast, primary osteomyelitis cases are reported to have a better outcome after surgical interventions, especially if sequestrectomy is performed.<sup>3</sup> However, this is at odds with our clinical experience, which is that cases of primary facial osteomyelitis have a high incidence of reinfection. It may be that incomplete bone debridement and curetting may leave behind infected fragments. On the other hand, extensive debridement of the affected area may be a risk factor for pathological fractures due to lack of remaining bone architecture. Recurrence of infections and risk of fractures represent a real challenge, but also an opportunity for new bone substrates capable of providing local delivery of antimicrobials and a scaffold for new bone formation in camelids.

Local antimicrobial delivery to affected tissues has been pioneered in human medicine with the use of PMMA or calcium sulphate beads<sup>18,19</sup> and subsequently developed in veterinary medicine,<sup>20</sup> where they are still largely investigational. Both antimicrobial impregnated PMMA or calcium sulphate beads have been reported with similar efficacy results.<sup>18</sup> However, while PMMA beads are indissolvable and require a second surgical intervention for their removal, calcium sulphate beads are slowly dissolvable, removing the need for a second surgical intervention. The latter is an important advantage in alpacas, which are highly susceptible to stress, especially when in hospital settings, and is a valuable option for improving patient management.

In addition to local antimicrobial delivery, calcium sulphate has been shown to provide a scaffold for new bone formation, together with improved bone angiogenesis.<sup>21</sup> Beads were preferred in this case because they are easily pressed into irregular spaces within and adjacent to bone. Bone scaffold formation is believed to be due to the well-orchestrated interaction between adhesion of osteoblasts onto the calcium sulphate substrate and reabsorption by osteoclasts.<sup>22</sup> This is a true advantage for reinforcing a much damaged bone surface with the aid of preventing weakening of the bone and pathological fractures.

Local delivery of antibiotics has been previously reported in the literature. It constitutes good clinical practice, allowing to reduce the risk of loco-systemic infection and consequently limiting systemic antimicrobials usage, however, necessary in the face of a surgical intervention. Although the exudate did not reveal a positive culture, both local and systemic antimicrobials were utilised in this case. It is known that bacteria are capable of invading the submicron osteocytic lacunar-canalicular system, which, despite the presence of infection, can yield a negative culture from the existing exudate<sup>23,24</sup>; however, as many cases with negative cultures recur in the face of treatment, this may indicate the presence of residual infection.

In this case report, the concomitant presence of the phlebitis provided sufficient clinical indication of local infection and warranted more aggressive treatment.

In hindsight, a culture of the curetted bone should have been performed; however, this would have delayed the application of the antimicrobial impregnated beads. In alternative, direct examination after staining of the pus could have also been performed to evaluate the presence of intracellular or extracellular bacteria.

In this case report, we elected to use a critically important antibiotic (CIA). The choice of utilising a CIA was dictated by the need of a water-soluble antimicrobial, essential requirement for substances that need to come in contact with bone surfaces. The scarce availability of water-soluble antimicrobials approved for farm animal use in the United Kingdom and its broad spectrum of action, made ceftiofur sodium, a third-generation cephalosporin (Excenel, Zoetis, UK), the drug of choice for this case. Within available water-soluble antimicrobials, trimethoprim sulfadiazines (TMS) or low-concentration oxytetracyclines could have been considered. However, as it is known, neither of the drugs represented an appropriate choice: TMS has limited pharmacological activity in purulent material and oxytetracyclines interact with calcium-rich substrates.

In this case report, despite the topical delivery of antimicrobials, the alpaca was continued to be treated systemically with florfenicol. Florfenicol has been previously reported to be used in alpacas with dental disease.<sup>6</sup> This drug, which was selected by the referring veterinarian after the initial and unsuccessful course of penicillin, was continued pre and post surgery. The decision of continuing this antimicrobial presurgically was dictated by allowing completing the course initiated by the referring veterinarian. The decision to continue the course postsurgically was made on the side of caution, given the pre-existing phlebitis and to eliminate the potential for septic emboli to disseminate and seed in other locations.

To the authors' knowledge, this is the first case report describing the successful use of calcium sulphate beads in primary facial osteomyelitis in alpacas. The positive results obtained in this case may be considered in the future for prevention of surgical complications in other primary osteomyelitis locations or in secondary osteomyelitis cases, after tooth removal is performed.

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The authors received no specific funding for this work.

## CONFLICT OF INTEREST

The authors declare they have no conflicts of interest. However, the authors wish to declare to have received the material at no cost from the manufacturer.

## ETHICS STATEMENT

Chronic facial osteomyelitis cases can have poor prognosis and may have high recurrence rate and secondary complications, such as mandibular fractures. To improve animal welfare and improve treatment outcome and reduce recurrence of infection, the authors utilised a medical device that was previously utilised in human medicine and in other

veterinary species. The aim of this treatment was not only to provide a local antimicrobial delivery to the affected site but also to create a ‘scaffolding’ for new bone regeneration. The authors confirm that this case report was written based on the treatment of a client-owned animal after receiving informed client consent. Except for the beads used in this case report, all drugs given were administered under the cascade. The client consented on the use of an off-licence medical device, confirming that the animal would not enter the food chain.

## ORCID

Eleonora Po  <https://orcid.org/0000-0002-9777-6707>

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